

Acuity Development in Infantile Nystagmus

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PURPOSE. To compare development of acuity in patients with isolated infantile nystagmus and infantile nystagmus associated with a visual sensory defect.

METHODS. Visual acuities in 57 children (1 month to 4 years of age) with infantile nystagmus were assessed by using Teller acuity cards oriented vertically during binocular viewing. Twenty-two had isolated infantile nystagmus, 21 had albinism, 7 had aniridia, and 7 had mild or moderate bilateral optic nerve hypoplasia (BONH). Longitudinal acuity was measured in 40 of these patients (mean 1.8, 2.3, 3.1, and 3.3, measurements per patient group, respectively). The rate of acuity development across the study groups was quantified by linear regression of log acuity versus log age and compared to published normative data.

RESULTS. The rate of acuity development was similar across all groups and paralleled the normative data. The slope of log grating acuity versus log age (\pm SEM) was normal, 0.73; isolated infantile nystagmus, 0.80 ± 0.11 ; albinism, 0.80 ± 0.11 ; aniridia, 0.87 ± 0.16 ; and BONH, 0.79 ± 0.18 . The slopes were not significantly different (ANCOVA, $F_{4,142} = 0.21$, $P = 0.93$). Compared with published binocular normative data, mean acuity adjusted for age was reduced by 1.2 octaves in isolated infantile nystagmus and by 1.7 to 2.5 octaves in nystagmus with associated sensory defect.

CONCLUSIONS. The rate of acuity development in infantile nystagmus is largely independent of the gaze-holding instability or an associated visual sensory defect. Reduction of mean acuity in albinism, aniridia, and BONH is due to the visual sensory defect and exceeds the acuity reduction observed in isolated infantile nystagmus. (*Invest Ophthalmol Vis Sci.* 2007;48:4093–4099) DOI:10.1167/iovs.06-1165

Infantile nystagmus (IN) refers to involuntary ocular oscillations that begin during the first 6 months of life.^{1,2} The oscillations are usually conjugate and horizontally directed in primary and eccentric gazes, but there can be a vertical or torsional component. Nystagmus amplitude typically increases with visual effort and dampens with convergence and sleep. Patients may adopt a head turn or tilt where the velocity of the nystagmus is minimized: the so-called null point. Despite the continuous eye movement, most patients do not perceive motion of their environment (oscillopsia). IN can appear as an isolated ocular motor abnormality with nearly normal acuity or in association with a visual sensory disorder including opacities of the ocular media (cornea, lens, or vitreous) and functional abnormalities of the macula (albinism and aniridia) or optic

nerve. Visual sensory disorders must be bilateral and present before 6 months of age to be associated with IN.¹ Eye movement recordings in adults with IN show either a horizontal pendular nystagmus, in which the left- and rightward phases of fast velocity are equal, or jerk nystagmus, in which the fast phase is in one direction.^{1,3} The mechanisms underlying IN are unknown. Investigators have described abnormalities in smooth pursuit, optokinetic, saccadic, and vestibulo-ocular subsystems.^{4–8} Jacobs and Dell'Osso⁹ have recently proposed a defect in smooth pursuit and gaze-holding ocular motor systems.

Nystagmus produces retinal image motion that can limit visual acuity. In normal adults, acuity is reduced with as little as 2 deg/s of retinal image motion.^{10–12} In infants, the decrease in acuity due to nystagmus must take into account normal visual development. In order for nystagmus to limit visual acuity development in infants, the motion blur from the nystagmus must exceed the immaturity limit of the visual system. Acuity is normally immature at birth and rapidly improves from 1 to 6 cyc/deg between 1 and 6 months of life.^{13–18} Spatial and temporal contrast sensitivity also improve rapidly during this period.^{19–23} Having lower acuity and contrast sensitivity, infants are likely to be more tolerant of retinal image motion than are adults. Although acuity development in IN has been investigated,^{24–30} few studies have provided quantitative analysis of acuity development compared with the norm.³¹

The relationship between acuity development and nystagmus is confounded by the nystagmus waveform and by age-related changes in the waveform.^{29,32,33} IN waveforms can be characterized as jerk or pendular. The jerk waveform is characterized by intrusion of a fast-phase component that places the object of regard on or near the fovea, followed by a slow-velocity component during which high-spatial-frequency components of stimuli are optimally sampled. Pendular nystagmus is characterized by a symmetric sinusoidal horizontal movement in which the visual system also uses the slow-velocity components to achieve optimal sampling of the object of regard. Although foveal and parafoveal sampling is a continuous process,^{34,35} high-spatial-frequency components are optimally sampled during low velocities.^{1,7,36} A limited number of studies have demonstrated that the pendular waveform can become asymmetric or evolve into a jerk nystagmus.^{29,32,33} Such age-related changes in the nystagmus waveform are possibly related to postnatal development of the macula or refinements of a preferred fixation locus in subjects with macular hypoplasia. At higher velocities, high-spatial-frequency stimuli are smeared, resulting in decreased acuity. Using eye tracking to quantify the relationship between acuity and image motion, Demer and Amjadi¹² found that there is a linear decrease in logMAR (logarithm of the minimum angle of resolution) acuity with increasing retinal slip velocity (retinal image velocity minus smooth pursuit velocity). In this paradigm, acuity was measured with the head fixed, whereas Snellen optotypes were sinusoidally drifted at peak velocities from 5 to 100 deg/s but were blanked during 50% of the duty cycle centered on turnaround points where velocity approaches zero.

The relationship between acuity development and IN is also confounded by the status of the visual sensory system. Visual acuity is reduced when there is an associated visual sensory disorder, such as albinism, aniridia, or bilateral optic nerve hypoplasia (BONH). The concurrent presence of nystagmus

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Supported by the William O. Rogers Trust Fund and by charitable contributions from Anderson and Peter G. La Haye.

Submitted for publication September 28, 2006; revised January 15, March 26, and May 4 and 25, 2007; accepted July 10, 2007.

Disclosure: **A.H. Weiss**, None; **J.P. Kelly**, None

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and a visual sensory disorder may impose multifactorial limitations on visual acuity development. In contrast, the finding that adults with IN have nearly normal acuity^{28,36,37} suggests that the nystagmus does not limit the development of acuity. The purpose of this study was to quantify and compare the rate of acuity development during early childhood in isolated IN and in IN associated with albinism, aniridia, and BONH.

METHODS

We retrospectively reviewed records of patients with IN syndrome who were seen between November 1991 and December 2005 at Children's Hospital and Regional Medical Center (Seattle, WA). The research adhered to the tenets of the Declaration of Helsinki, and chart review was approved by the institutional review board (IRB). The inclusion criterion was the appearance of conjugate jerk nystagmus or pendular nystagmus in the first 6 months of life. Evaluation included a comprehensive eye examination before 14 months of age; Teller acuity card (TAC) testing; cycloplegic retinoscopy; assessment of eye alignment, eye movements, and pupillary responses; slit lamp evaluation; and dilated fundus examination by direct and indirect ophthalmoscopy. Patients with IN were categorized into one of the following four groups: (1) isolated IN, or IN associated with (2) aniridia, (3) albinism, or (4) BONH. Of the 57 patients enrolled in the study, 22 had isolated IN, 21 had albinism (16, oculocutaneous albinism; 5, ocular albinism), 7 had aniridia, and 7 had mild to moderate BONH. Exclusion criteria were opacifications of the ocular media, unilateral optic nerve disorders, severe bilateral optic nerve disorders, glaucoma, optic nerve coloboma, and structural and functional retinal disorders other than macular hypoplasia. None of the patients had systemic or neurologic disease except for three patients with optic nerve hypoplasia.

Clinical Examination

Isolated IN was diagnosed on the basis of normal findings in a fundus examination and family history (2 patients) or normal full-field ERG (20 patients). ERG recordings followed ISCEV (International Society for Clinical Electrophysiology of Vision) protocols³⁸ and were performed with the patient under chloral hydrate sedation (75 mg/kg). Details of the ERG recordings are described elsewhere.³⁹ Although the full-field ERG is sensitive to cone dysfunction, it does not exclude subclinical abnormalities limited only to the macula.

The diagnosis of albinism was based on clinical detection of macular hypoplasia in association with iris transillumination defects and RPE hypopigmentation. Oculocutaneous albinism was distinguished by the presence of hypopigmentation of skin and hair and autosomal recessive inheritance. Ocular albinism was diagnosed on the basis of normal skin and hair pigmentation, iris transillumination defects, maternal presence of patchy hypopigmentation of the RPE or skin, X-linked inheritance, or genetic testing. Strabismus was noted in 3 of 21 patients. One of the patients had Angleman syndrome. None of the remaining patients had findings consistent with Prader-Willi, Chediak-Higashi, or Hermansky-Pudlak syndromes.

The diagnosis of aniridia was based clinically on the congenital presence of a bilateral annular deficiency of the central iris along with macular hypoplasia. Molecular detection of a *PAX6* mutation was documented in two patients. None of the patients had Wilms' tumor or WAGR (Wilms' tumor, aniridia, and genitourinary abnormalities with mental retardation) syndrome.

The diagnosis of BONH was based on ophthalmoscopic detection of an abnormally small optic disc with an estimated disc diameter of $\leq 1200 \mu\text{m}$.⁴⁰ Additional ophthalmoscopic evidence of BONH included disc pallor, the "double-ring" sign, and segmental irregularities of the disc margins. To minimize the inclusion of patients with cortical visual impairment, we excluded those with structural cortical abnormalities. To be included in the study, patients had to have mild or moderate BONH and TAC acuity of 3 cyc/deg or better at the most recent examination. These criteria were selected to match the acuity deficits

observed in the patients with aniridia or albinism, but will bias the results for this population. Children with severe vision loss represented a separate subgroup who failed to show any appreciable postnatal improvements in acuity.²⁶ Six of seven patients had a brain CT ($n = 1$) or MRI ($n = 5$). Imaging was normal in three patients and demonstrated a small anterior pituitary and/or posterior bright spot in three patients.

Visual Acuity

All patients had acuity assessments using the TACs. Testing was conducted according to published methods¹⁴ at age-appropriate viewing distances, and results were compared to published normative data.^{17,18} In brief, the child is presented with a gray card containing a grating on one side that is matched in mean luminance to the gray background. In the standard protocol, the location of a vertical grating is randomly switched to the left or right of central gaze. Often, it was difficult to disambiguate a voluntary gaze shift to the pattern grating from a shift caused by the underlying nystagmus. Therefore, visual acuity was tested with the TACs held vertically so that the gratings were horizontally oriented.⁴¹ Binocular acuity was tested first, and if tolerated, monocular testing was then attempted. All testers had extensive experience with acuity card testing. Approximately 90% of the acuities were measured by one tester (JK). Patients with an eccentric or tilted head posture had visual acuity tested in their preferred head position.

Criteria for optical correction were stratified according to age. Patients older than 3 years were tested with their full optical correction if they met the following criteria: (1) tolerated wearing correction and (2) had myopia worse than -1.00 D in spherical equivalent, or (3) hyperopia greater than $+5.00$ D in spherical equivalent, or (3) astigmatism (in plus cylinder notation) of 1.5 D or more. Patients less than 3 years of age are typically intolerant of glasses. Therefore, we attempted to measure acuity with optical correction when refractive error was more than 3 D of myopia in spherical equivalent or more than 5 D of hyperopia in spherical equivalent. The number of subjects who met the criteria for optical correction was 1 of 22 with isolated IN, 5 of 21 with albinism, 0 of 7 with aniridia, and 5 of 7 with BONH. Of the 11 who met the optical criteria, 5 were tested with correction; the remaining 6 (1 with albinism, 5 with BONH) were intolerant of correction, primarily because of age or developmental delay. One subject with isolated IN was tested without correction on the first visit and with correction on two subsequent visits.

Anisometropia of less than 0.50 D in spherical equivalent was present in 20 of 22 patients with isolated IN, 17 of 21 with albinism, 5 of 7 with aniridia, and 4 of 7 with BONH. Anisometropia between 0.50 and 2.00 D spherical equivalent was present in 2 patients with isolated IN, 4 with albinism, 2 with aniridia, and 2 with BONH. Anisometropia of greater than 2.00 D spherical equivalent was present in 1 patient with BONH. The relationship between uncorrected refractive error and monocular TAC acuity across ages is examined in the Results section.

Forty of 57 infants had two or more acuity assessments. The remaining 17 infants lacked longitudinal acuity assessments because of limited follow-up or missed clinical appointments. Only binocular viewing data were analyzed for developmental trends in acuity.

RESULTS

Table 1 summarizes age, number of visits, and refraction, stratified by patient group. The number of longitudinal acuity measurements ranged from two to four for patients with isolated IN, and from two to five for patients with albinism, aniridia, or BONH. Refractive error in Table 1 represents one data point for each subject, with the refraction taken at the oldest age, since it is the most reliable reading and reflects age-related changes. Three of 21 subjects with albinism had strabismus. Clinical assessment revealed a horizontal conjugate pendular or jerk nystagmus with amplitudes ranging from 2° to

TABLE 1. Summary of Patient Data

	Isolated IN	Albinism	Aniridia	BONH
Patients (<i>n</i>)	22	21	7	7
Visits (<i>n</i>)	40	50	22	23
Mean visits per patient	1.8	2.3	3.1	3.3
Mean age (y) at presentation	0.69	0.48	0.68	0.49
Mean age (y) across all visits	2.91	2.71	2.63	3.27
Mean spherical refraction right and left eye*	0.80	0.39	0.70	-4.32
Spherical refraction (SD) right and left eye	1.38	4.77	3.42	5.02
Mean astigmatism right and left eye	0.63	0.74	0.68	1.29
Astigmatism (SD) right and left eye	0.75	0.82	1.42	0.92
Mean astigmatism axis	88	100	87	69
Range of spherical error*	-2.50 to +4.25	-10.50 to +6.50	-9.50 to 5.50	-12.50 to +4.00
Range of astigmatism	Plano to +2.50	Plano to +2.25	Plano to +4.00	Plano to +3.00

* Absolute sphere.

30° and frequencies ranging from 0.3 to 3 Hz across all patient groups.

Figure 1 shows binocular acuity, both cross-sectional and longitudinal, for all subjects during the first 4 years of life. For comparison, the gray area represents the tolerance limits in 90% of the population with 95% probability (or 90% probability for infants <4 months of age).¹⁸ The tolerance limits cover 90% of the population and exclude 5% above the upper limit and 5% below the lower limit. A subset of individuals in each patient group had acuities that overlapped the normative data or fell near the lower 5% tolerance limit. Subjects with isolated IN showed the most overlap with the normative data; 14 (64%) of 22 subjects had at least one acuity measurement within the normal range. In the remaining groups, the number of subjects

with at least one acuity measurement falling within the tolerance limit of normal data was 10 (48%) of 21 patients with albinism, 2 (28%) of 7 patients with aniridia, and 1 (14%) of 7 patients BONH.

Four patients in Figure 1 (two with albinism, one with aniridia, and one with BONH) initially showed no orientation to the low-vision card before 5 months of age. These initial data points are arbitrarily plotted at 0.10 cyc/deg but were excluded from subsequent data analysis. Another patient with BONH initially oriented to only the largest grating (0.22 cyc/deg). All these patients showed rapid improvement in acuity after 6 months of age, consistent with delayed visual maturation.^{25,26} Two patients had hyperopic refractions (right eye and left eye, respectively, +1.75, +1.50 sphere and +4.50 +2.00 × 90,

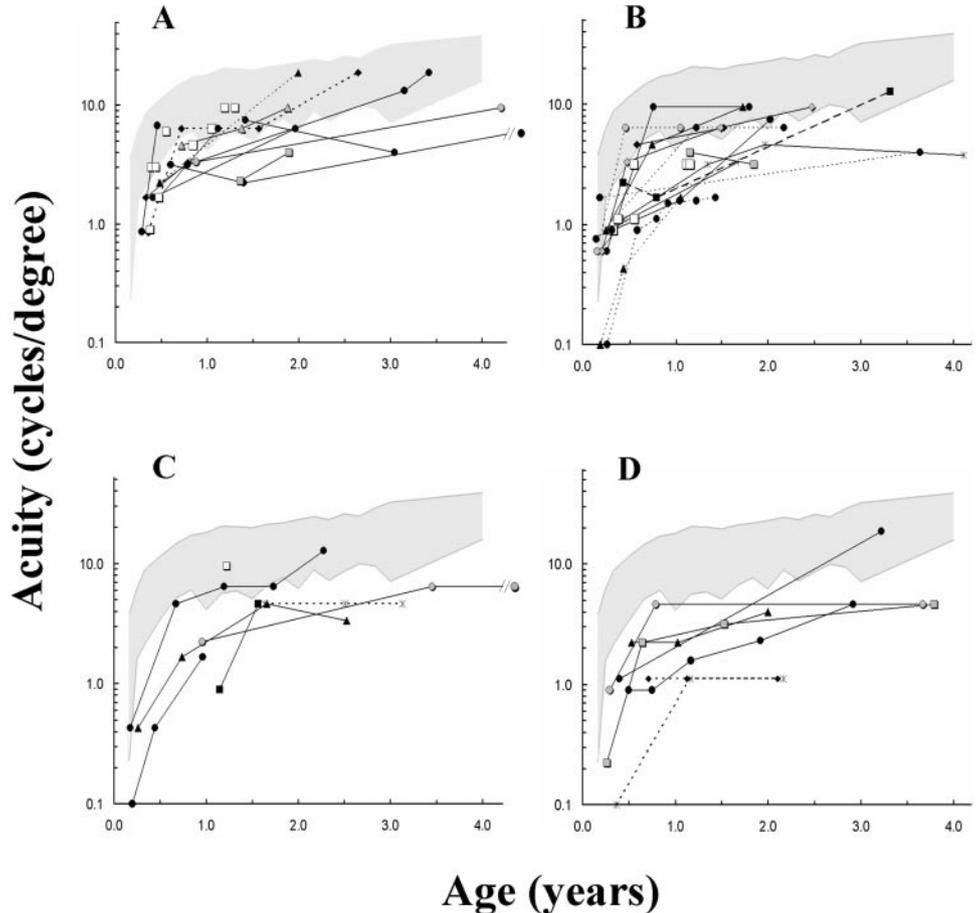


FIGURE 1. Development of binocular grating acuity measured with TACs in children with infantile nystagmus. *Open squares*: cross-sectional data; *symbols connected by lines*: longitudinal data from individual subjects. Infants lacking visual orientation to the low-vision card are arbitrarily plotted at 0.10 cyc/deg. Patients were separated into four diagnostic groups (A) isolated infantile nystagmus, (B) albinism, (C) aniridia, and (D) BONH. *Shaded area*: tolerance limits of normal binocular acuity.¹⁸

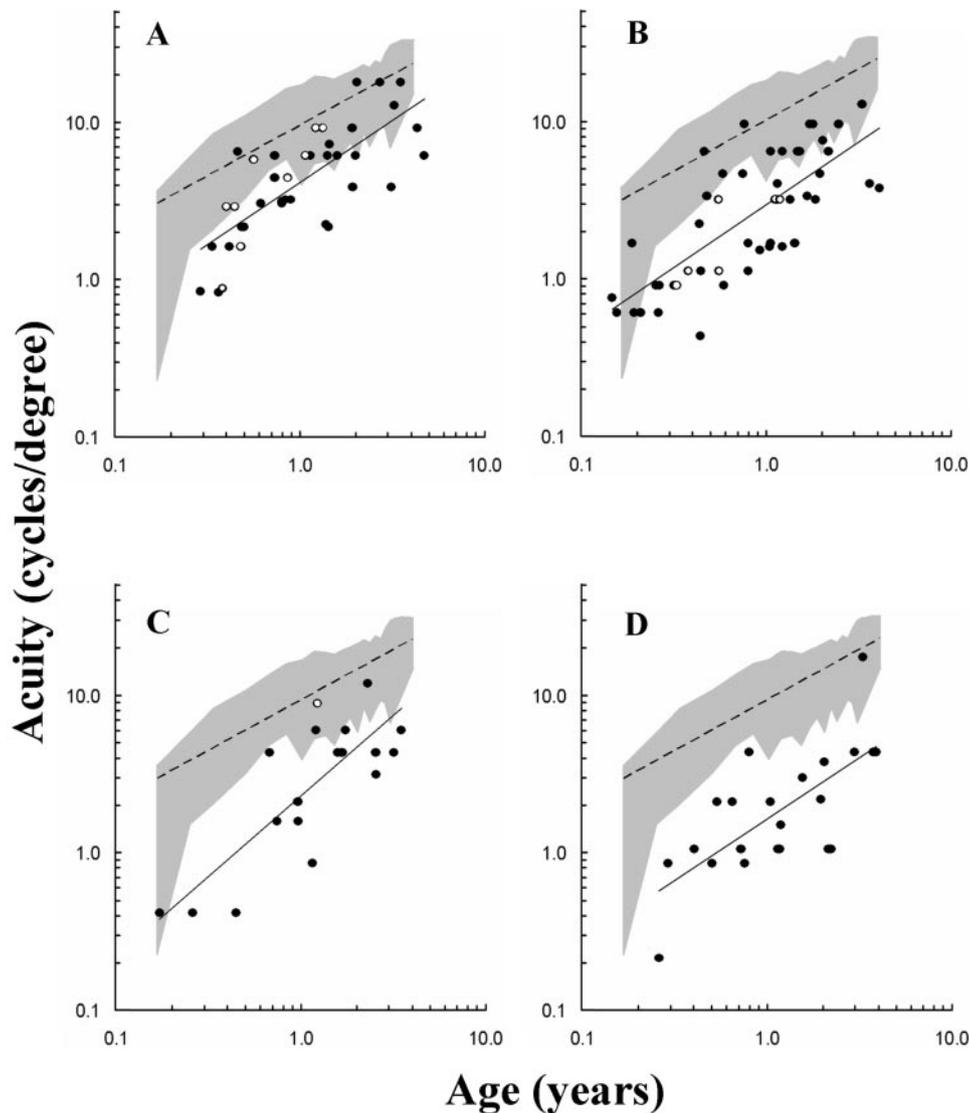


FIGURE 2. Binocular grating acuity is plotted on a log-log scale to demonstrate the linear relationship between acuity and age. Patients were separated into four diagnostic groups: (A) isolated infantile nystagmus, (B) albinism, (C) aniridia, and (D) BONH. *Shaded area:* tolerance limits of normal binocular acuity.¹⁸ *Solid lines:* linear regression of the patient data; *dotted lines:* regression to the normative data. (○) Cross-sectional data; (●) longitudinal data.

+3.50 + 2.00 × 90), and three had myopic refractions (−6.00, −6.00 sphere; −4.50 + 1.00 × 90, −4.50 + 1.00 × 90; and −3.75 + 2.75 × 105, −3.75 + 2.25 × 75).

The relationship between acuity development and age was further examined by plotting the patient data and age-matched normal data on a log-log scale (Fig. 2). Both cross-sectional and longitudinal data were used in the analysis. Log acuity in-

creased linearly with log age in all patient groups. Correlation coefficients were highly significant for each group ($P < 0.01$; $F > 19.0$). The slope, standard errors of the slope, r^2 values, and sample size are shown in Table 2. The slopes of the regressions for all patient groups are within one SE of normative data, indicating that the regression lines are nearly parallel. Variation from the regression line was within 1 log unit for

TABLE 2. Slope of Binocular Acuity Development in Log-Log Scale

Patient Group	Slope	SE	r^2	Sample (n)
Birth to 4 years				
TAC norms ¹⁸	0.73	0.04	0.95	21*
Isolated infantile nystagmus	0.80	0.11	0.57	40
Albinism	0.80	0.11	0.56	48
Aniridia	0.87	0.16	0.62	21
BONH	0.79	0.18	0.49	22
Birth to 1 year				
TAC norms ¹⁸	0.95	0.05	0.98	8*
Isolated infantile nystagmus	1.26	0.31	0.46	21
Albinism	0.86	0.26	0.32	25
Aniridia	1.15	0.39	0.63	7
BONH	1.45	0.55	0.49	9

* Sample size represents the number of age-specific groups into which 646 subjects in Salomão and Ventura¹⁸ were binned and then averaged.

isolated IN and up to 1.5 log units for nystagmus with visual sensory disorders. To analyze the slopes of acuity development further across patient groups, we used analysis of covariance (ANCOVA). The ANCOVA interaction was not statistically significant, indicating that the rates of acuity development with age, represented by the slopes of the regression lines in Table 2, were not different across patient groups and normative data ($F_{4,142} = 0.212$; $P = 0.931$).

Because acuity is highly dependent on age during the first 4 years, mean acuity in each patient group is influenced by the distribution of ages. Because there is no significant interaction, ANCOVA was also used to test for mean differences in acuity between patient groups using age as a covariate. The ANCOVA main effect was significant ($F_{4,142} = 29.3$; $P < 0.0001$). Compared with published norms, relative reductions in log acuity (differences in marginal means with the Bonferroni correction) were -0.351 ($P < 0.001$) for isolated IN, -0.522 ($P < 0.001$) for albinism, -0.618 ($P < 0.001$) for aniridia, and -0.748 ($P < 0.001$) for BONH. The magnitude of acuity reduction is analogous to the offsets of the y -intercepts of the regression lines when the covariates have the same slopes (cf. Keppel⁴²). The average acuity reduction in patients with associated visual sensory disorders was uniformly 1 to 2 octaves, which is larger than test-retest variability in a clinical population.^{14,43} All subject groups with visual sensory defects showed significant reduction in acuities when compared to those with isolated IN ($P < 0.02$ for each comparison with Bonferroni correction).

To determine whether early visual development was differentially reduced, we similarly analyzed the data from birth to 1 year of age. The bottom half of Table 2 shows the regression data for these subjects. Although the slope of acuity development is uniformly higher in the first year than in the period from birth to 4 years, the variation in slopes overlap each other. The ANCOVA interaction is not significant ($F_{4,60} = 0.45$; $P = 0.77$), indicating the rates of acuity development with age, represented by the slopes of the regression lines in Table 2, were not different across groups. The observed power for the interaction was low at 0.149, which is the probability of correctly detecting significantly different slopes at the 0.05 level. The ANCOVA main effect of patient group was significant ($F_{4,60} = 5.1$; $P < 0.01$). Compared with normative data, mean reduction in acuity was 0.49 log unit for isolated IN ($P < 0.01$), 0.62 log unit for albinism ($P < 0.001$), 0.83 log unit for aniridia ($P < 0.001$), and 0.81 log unit for BONH ($P < 0.001$). Furthermore, on average, the five patients with delayed visual maturation subsequently had slopes in acuity development that overlapped the distribution of the remaining patients with nystagmus ($1.05, \pm 0.19$ vs. 0.890 ± 0.34 SEM).

Figure 3 plots the combined TAC data from Summers³¹ (40 subjects) and Whang et al.⁴⁴ (64 subjects) for children with albinism compared with the data from the present study. The regression line for our albinism patients nearly matches the slope of the regression line of the published measurements. The slope for the combined Summers³¹ and Whang et al.⁴⁴ data is 0.73 ± 0.06 ($r^2 = 0.92$), compared with the slope of 0.80 ± 0.11 in our subjects with albinism.

Figure 4 shows the relationship between refractive error and monocular acuity in subjects with isolated IN who were tested without correction. Only subjects with isolated IN were included in this analysis, to remove the potential confound of a visual sensory defect. Age-related differences were accounted for by plotting acuity in octaves relative to the lower 2.5% prediction limits of the published monocular norms.¹⁷ Because the normative data contain only values at discrete ages, we interpolated values specific to each patient's age. The acuity of the right eye was plotted except in two cases of anisometropia in which the left eye (with the lesser spherical equivalent refractive error) was plotted. In Figure 4A, relative reduction in

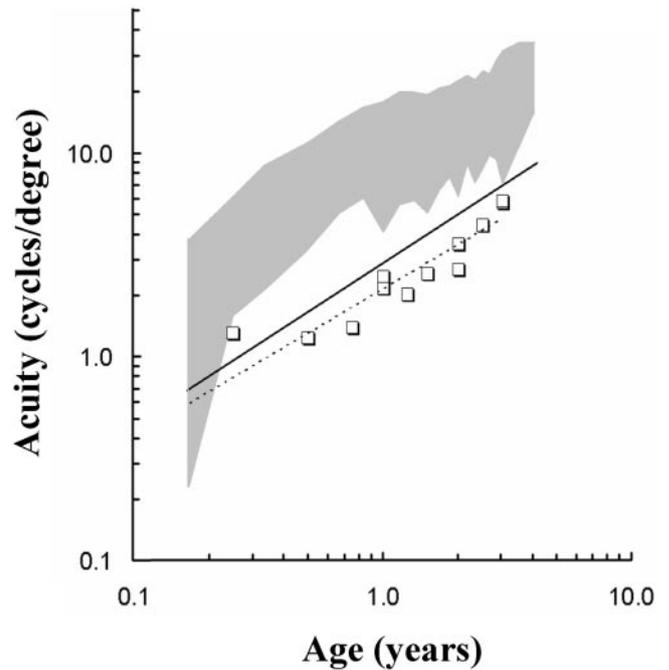


FIGURE 3. Acuities in children with albinism are compared to the acuity data from Summers³¹ and Whang et al.⁴⁴ *Solid regression line*: average of subjects in current study; *dotted regression line*: the fitted regression to the combined data from Whang et al. and Summers (*open squares*). *Shaded area*: tolerance limits of normal binocular acuity.¹⁸

acuity versus spherical equivalent refractive error is plotted for 28 measurements from 22 subjects. No correlation was found between the spherical equivalent and relative acuity reduction ($r^2 = 0.07$; $P = 0.18$). In Figure 4B, 14 measurements from 13 subjects with 0.5 D or more of with-the-rule or against-the-rule astigmatism are plotted for relative reduction in acuity versus astigmatism. Subjects without astigmatism are plotted as filled circles. Two subjects with astigmatism along the 45° axis were removed from the analysis. No correlation was found between astigmatism and relative acuity reduction ($r^2 = 0.01$; $P = 0.731$). Furthermore, the distribution of acuities in subjects with astigmatism was not significantly different from that in subjects without astigmatism ($P = 0.89$; t -test). Only one subject had astigmatism along the 180° axis (Fig. 4B, filled diamond).

DISCUSSION

Despite having continuous eye movements, subjects with IN demonstrated postnatal improvements in visual acuity that parallel improvements shown by age-matched normal subjects. This conclusion is based on the observation that the slopes of acuity development are the same for normal subjects and subjects with isolated IN or IN with associated visual sensory disorders. We propose that, for postnatal acuity development to follow the normal trajectory, acuity development is interdependent on the slow phase of eye movement. Visual signals are known to exert control on ocular motor behavior, but evidence is also emerging that the ocular motor signals provide feedback to early visual areas that improve visual performance.^{45,46}

In patients with isolated IN, visual acuity was reduced by 1.5 octaves in the first year of life and was reduced on average by 1 octave during the first 4 years of life. This reduction in acuity approximates the average acuity reduction also reported in adults with isolated IN.^{28,36,47} Given that infants have much

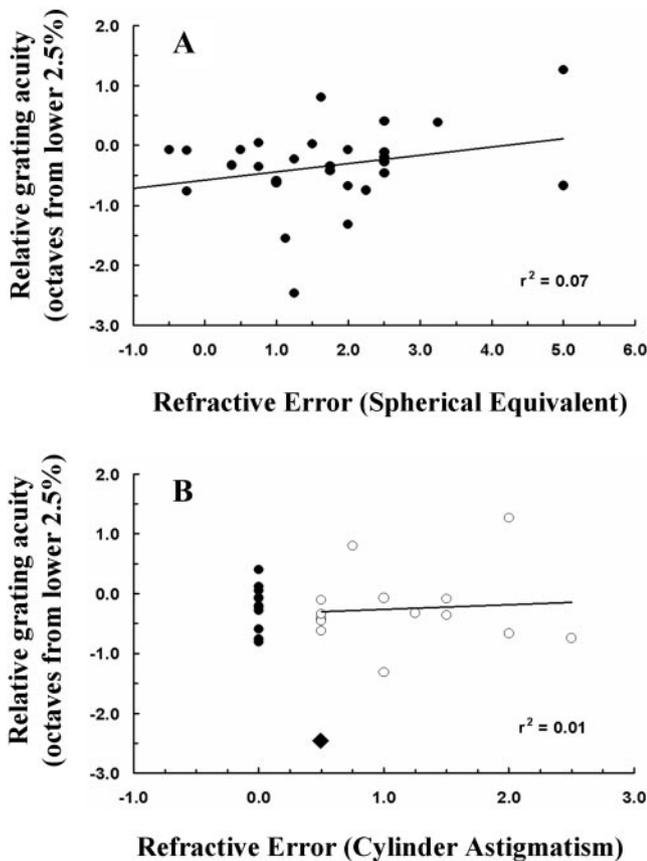


FIGURE 4. The relationship between refractive errors and monocular acuity reduction in subjects with isolated IN who were tested without correction. Age-related differences in acuity were accounted for by plotting monocular acuity in octaves relative to the lower 2.5% prediction limit of age-normative acuity.¹⁷ (A) Regression of refractive error in spherical equivalent versus acuity reduction. (B) Regression of astigmatic refractive error versus acuity reduction. (○) Subjects with astigmatism along 90° ($\pm 20^\circ$) axis (with regression line). (▲) One subject with astigmatism along the 180° axis. (●) Monocular data in subjects without astigmatism.

lower acuity, we would expect greater tolerance for retinal image motion, with no impact on acuity. We postulate several mechanisms for the acuity reduction during visual development. First, temporal contrast sensitivity is immature within the same temporal frequencies of the oscillations observed in IN,^{22,48,49} but may be further reduced in these patients. Second, foveal immaturity imposes not only a spatial limitation due to lower cone photoreceptor density but also a reduction in quantal efficiency due to immature photoreceptor outer and inner segments⁵⁰ (i.e., lower pigment density and poorer waveguide properties). Third, immaturities in postreceptoral mechanisms from retina to cortex involved in higher level visual processing may be vulnerable to the effects of nystagmus. Fourth, abnormal motion signals generated by IN could add noise to visual processing, thereby reducing the signal-to-noise ratio and sensitivity of the spatial sampling mechanism. Supportive evidence comes from physiological studies showing that fixation instability increases response variability in primary visual cortex.⁵¹ Last, the possibility that subjects with isolated IN have a subclinical macular disorder cannot be completely excluded.

IN with visual sensory disorder was uniformly associated with reduced acuity across ages but a normal rate of acuity development. This finding suggests that the reduced acuities of patients with visual sensory-associated nystagmus are best

accounted for by the underlying visual sensory disorder not the gaze-holding instability. In albinism and aniridia, macular hypoplasia is likely to be the underlying sensory defect.⁵²⁻⁵⁵ Although BONH is characterized by a selective reduction in retinal ganglion cells,⁵⁶ the presumed loss of their connections to macular cone photoreceptors would indirectly set a lower acuity limit. Owing to the lower acuity in these patients, the nystagmus slow-phase velocity and tolerance for retinal image motion is likely to be higher in IN with visual sensory disorders than in isolated IN and normal infant vision.

Our use of horizontally oriented gratings rather than the standard vertically oriented gratings for TAC measurements deserves further discussion. We selected a horizontally oriented grating for two reasons. First, orienting the TACs vertically allowed the tester to disambiguate the patient's gaze direction from the underlying horizontal nystagmus. Second, horizontal gratings have been shown by investigators to provide an optimal stimulus for a patient with horizontal nystagmus.^{31,41,57,58} During horizontal nystagmus, the high contrast at the black-white edges of a vertical grating appears smeared. In comparison, contrast along the edges of a horizontal grating remains constant during horizontal nystagmus. As evidence, adults with IN and albinism have impaired sensitivity for vertically oriented stimuli, even for briefly flashed targets in which there is no retinal motion.^{31,57,59-61}

Five (9%) of 57 patients, all less than 6 months of age, did not orient to the low-vision card or responded only to the largest grating (0.22 cyc/deg) but then demonstrated significant acuity improvements after 6 months of age. These visual delays were found only in patients with an associated visual sensory defect and are consistent with reports of delays in visual maturation in the context of albinism or IN.^{25,26} After the catch-up phase the slopes of acuity improvement did not differ from the remaining 91% of patients. Because acuity in infants with delayed visual maturation overlaps the acuities in infants with Leber's congenital amaurosis and severe optic nerve hypoplasia,²⁶ repeat TAC measurements to document delayed improvements after 6 months of age are essential.

In summary, acuity development in children with IN, with or without associated visual sensory disorders, parallels normal acuity development. Retinal image motion due to nystagmus alone is associated with an average reduction of one octave in mean acuity, regardless of age. Our data suggest that reduced acuity in subjects with IN with associated visual sensory defect is primarily limited by the macular hypoplasia or optic nerve dysfunction. The relationship between acuity and the velocity profile of the nystagmus deserves further investigation.

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